

Amendments to the Specification:

Please amend the Specification as follows:

On **page 1**, please delete the paragraph between the title of the Invention, that is **METHODS AND COMPOSITIONS FOR DETECTING TARGET SEQUENCES**, and the **FIELD OF THE INVENTION**, and replace it with the following amended paragraph:

This application is a continuation-in-part of ~~co-pending application serial no. 09/350,309, which is a divisional application U.S. Patent No. 5,985,557, and is also a continuation-in-part of co-pending application serial no. 09/381,212 which is a national entry of PCT application no. US 98/05809, which claims priority to U.S. Patent Nos. 5,994,069, 6,090,543, 5,985,557, 6,001,567, and 5,846,717 and PCT application no. US 97/01072.~~ U.S. 09/381,212 filed February 8, 2000, which claims priority to PCT/US98/05809 filed March 24, 1998, which is a PCT application that claims priority to U.S. 08/823,516 filed March 24, 1997, now issued as U.S. 5,994,069 on November 30, 1999, which is continuation-in-part of U.S. 08/759,038 filed December 2, 1996, now issued as U.S. 6,090,543 on July 18, 2000, which is a continuation-in-part of U.S. 08/756,386 filed November 29, 1996, now issued as U.S. 5,985,557 on November 16, 1999, which is a continuation-in-part of U.S. 08/682,853 filed July 12, 1996, now issued as U.S. 6,001,567 on December 14, 1999, which is a continuation-in-part of U.S. 08/599,491 filed on January 24, 1996, now issued as U.S. 5,846,717 on December 8, 1998. This application is also a continuation-in-part of U.S. 09/350,309 filed on July 9, 1999, now issued as U.S. 6,348,314 in February 19, 2002, which is a divisional application of U.S. 08/756,386 filed November 29, 1996, now issued as U.S. 5,985,557 on November 16, 1999.

On **page 42**, please delete the sentence of lines 19-21, and replace it with the following amended sentence:

The degree of overlap will vary depending upon the nature of the complementarity (see, e.g., region "X" in Figs. ~~29~~25 and 67 and the accompanying discussions).

On **page 73**, please delete the sentences of lines 1-21, and replace them with the following sentences:

Certain preferred embodiments of the invasive cleavage reactions are provided in the following descriptions. As exemplified by the diagram in Fig. ~~29~~25, the methods of the present invention employ at least a pair of oligonucleotides that interact with a target nucleic acid to form a cleavage structure for a structure-specific nuclease. In some embodiments, the cleavage structure comprises i) a target nucleic acid that may be either single-stranded or double-stranded (when a double-stranded target nucleic acid is employed, it may be rendered single stranded, *e.g.*, by heating); ii) a first oligonucleotide, termed the "probe," that defines a first region of the target nucleic acid sequence by being the complement of that region (regions X and Z of the target as shown in Fig. ~~29~~25); iii) a second oligonucleotide, termed the "INVADER," the 5' part of which defines a second region of the same target nucleic acid sequence (regions Y and X in Fig. ~~29~~25), adjacent to and downstream of the first target region (regions X and Z), and the second part of which overlaps into the region defined by the first oligonucleotide (region X depicts the region of overlap). The resulting structure is diagrammed in Fig. ~~29~~25.

While not limiting the invention or the instant discussion to any particular mechanism of action, the diagram in Fig. ~~29~~25 represents the effect on the site of cleavage caused by this type of arrangement of a pair of oligonucleotides. The design of such a pair of oligonucleotides is described below in detail. In Fig. ~~29~~25, the 3' ends of the nucleic acids (i.e., the target and the oligonucleotides) are indicated by the use of the arrowheads on the ends of the lines depicting the strands of the nucleic acids (and where space permits, these ends are also labeled "3").

On **Page 74**, please delete the sentence of lines 2-5 and replace it with the following amended sentence:

Neither diagram (*i.e.*, Fig. ~~29~~ 25 or Fig. 32c) is intended to represent the actual mechanism of action or physical arrangement of the cleavage structure and further it is not intended that the method of the present invention be limited to any particular mechanism of action.

On **page 77**, please delete the sentence of lines 11-13, and replace it with the following amended sentence:

One way of accomplishing such turnover, where the INVADER oligonucleotide and probe oligonucleotide share a region of complementarity, can be envisioned by considering the diagram in Fig. ~~29~~ 25.

On **page 95**, please delete the sentence of lines 6-10, and replace it with the following amended sentence:

As demonstrated below, in one embodiment, reactions can be performed under conditions that prevent the cleavage of probes bearing even a single-nucleotide difference mismatch within the region of the target nucleic acid termed "Z" in Fig. ~~29~~ 25, but that permit cleavage of a similar probe that is completely complementary to the target in this region.

On **page 49**, please delete the sentence of lines 6-7, and replace it with the following amended sentence:

Fig. 21B shows that the "nibbling" of Fig. ~~25A~~ 21A is 5' nucleolytic cleavage and not phosphatase cleavage.